

# **EXHIBIT E**



US005795716A

**United States Patent** [19]

Chee et al.

[11] Patent Number: **5,795,716**[45] Date of Patent: **Aug. 18, 1998**

[54] **COMPUTER-AIDED VISUALIZATION AND ANALYSIS SYSTEM FOR SEQUENCE EVALUATION**

WO 92/10588 6/1992 WIPO .  
95/11995 5/1995 WIPO .  
WO 95/35505 12/1995 WIPO .

[76] Inventors: **Mark S. Chee**, 3199 Waverly St., Palo Alto, Calif. 94306; **Robert J. Lipshutz**, 970 Palo Alto Ave., Palo Alto, Calif. 94381

[21] Appl. No.: **327,525**

[22] Filed: **Oct. 21, 1994**

[51] Int. Cl.<sup>6</sup> ..... **C12Q 1/68; C12P 19/34; G06F 15/46; C07H 21/04**

[52] U.S. Cl. .... **435/6; 435/91.1; 435/91.2; 382/178; 382/179; 364/96; 364/97; 364/98; 364/99; 536/24.3; 536/24.33; 536/24.32; 536/23.1**

[58] Field of Search ..... **382/178, 179; 435/5, 6, 91.2, 91.1, 7.1, 7.2, 23.1; 536/24.3, 24.33, 96, 97, 98, 99**

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Primary Examiner—W. Gary Jones

Assistant Examiner—Dianne Rees

[57] **ABSTRACT**

A computer system for analyzing nucleic acid sequences is provided. The computer system is used to perform multiple methods for determining unknown bases by analyzing the fluorescence intensities of hybridized nucleic acid probes. The results of individual experiments are improved by processing nucleic acid sequences together. Comparative analysis of multiple experiments is also provided by displaying reference sequences in one area and sample sequences in another area on a display device.

**10 Claims, 26 Drawing Sheets**

**Microfiche Appendix Included**  
(5 Microfiche, 272 Pages)

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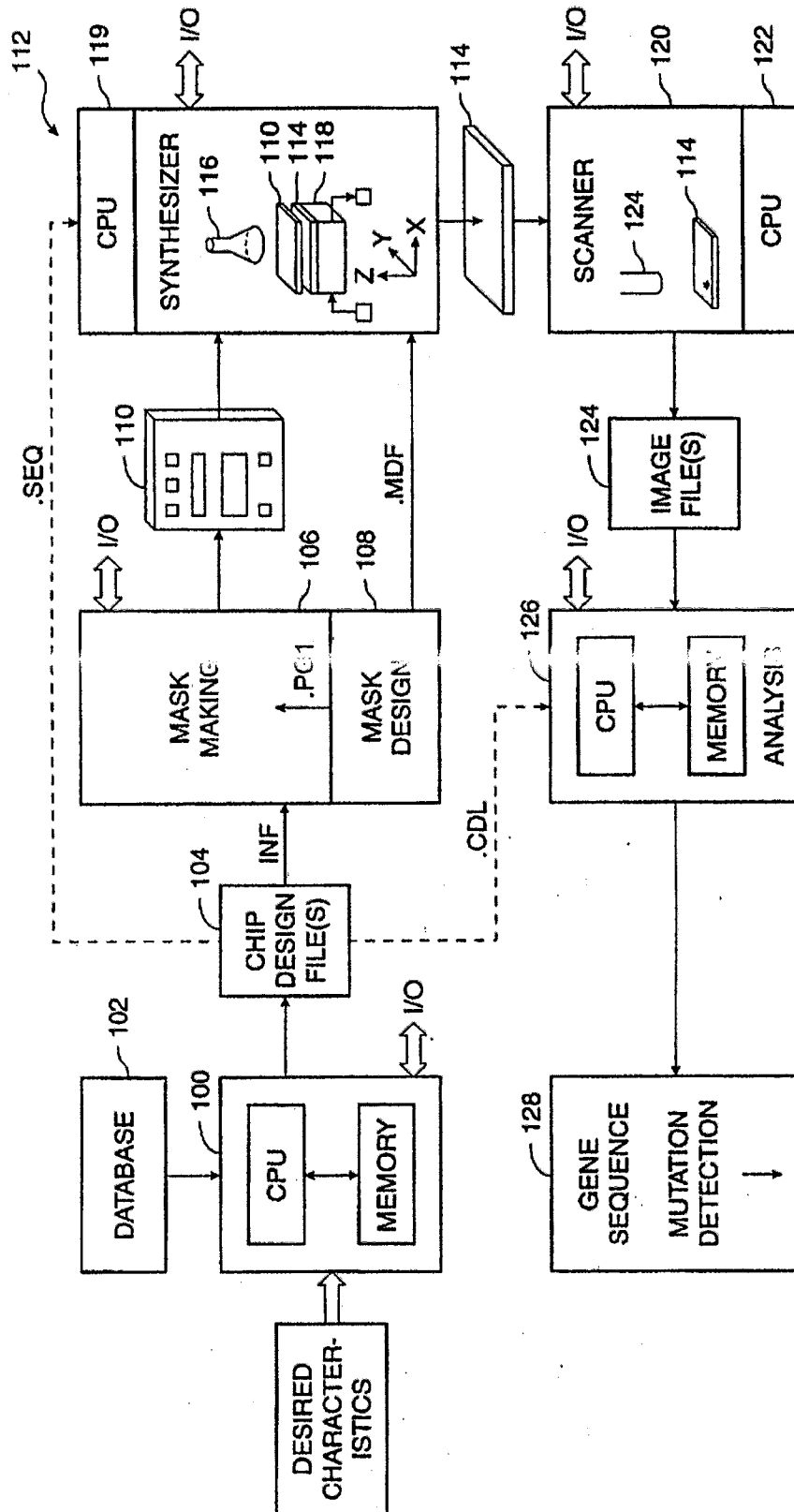


FIG. 1

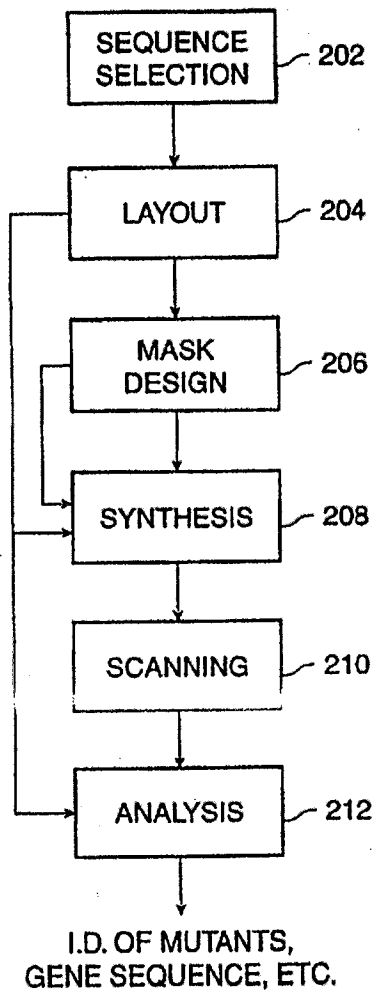


FIG. 2A

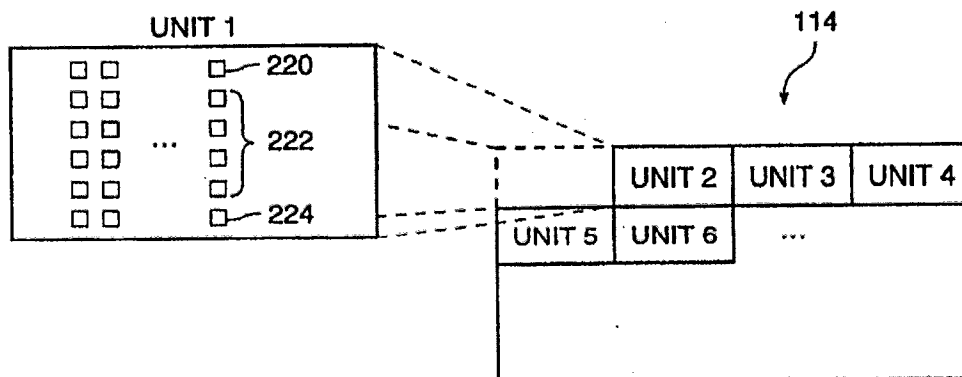


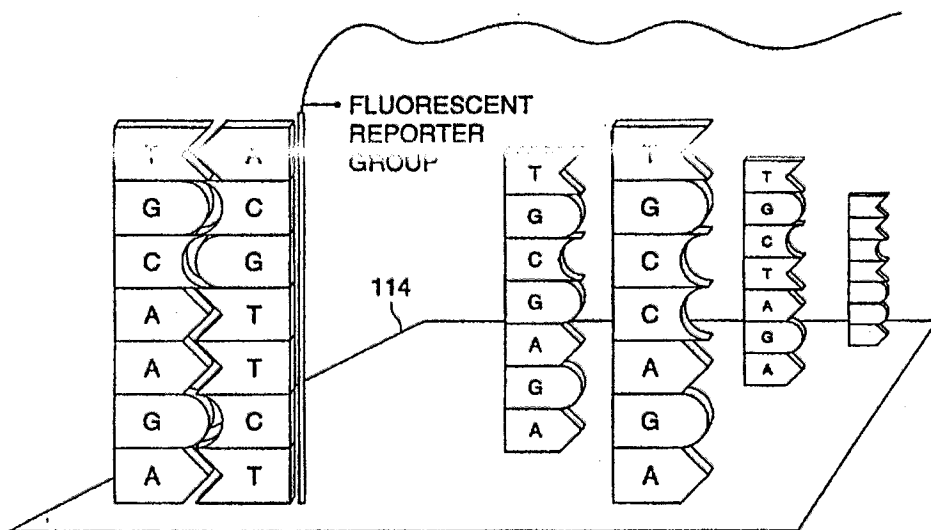
FIG. 2B

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**FIG. 2C**

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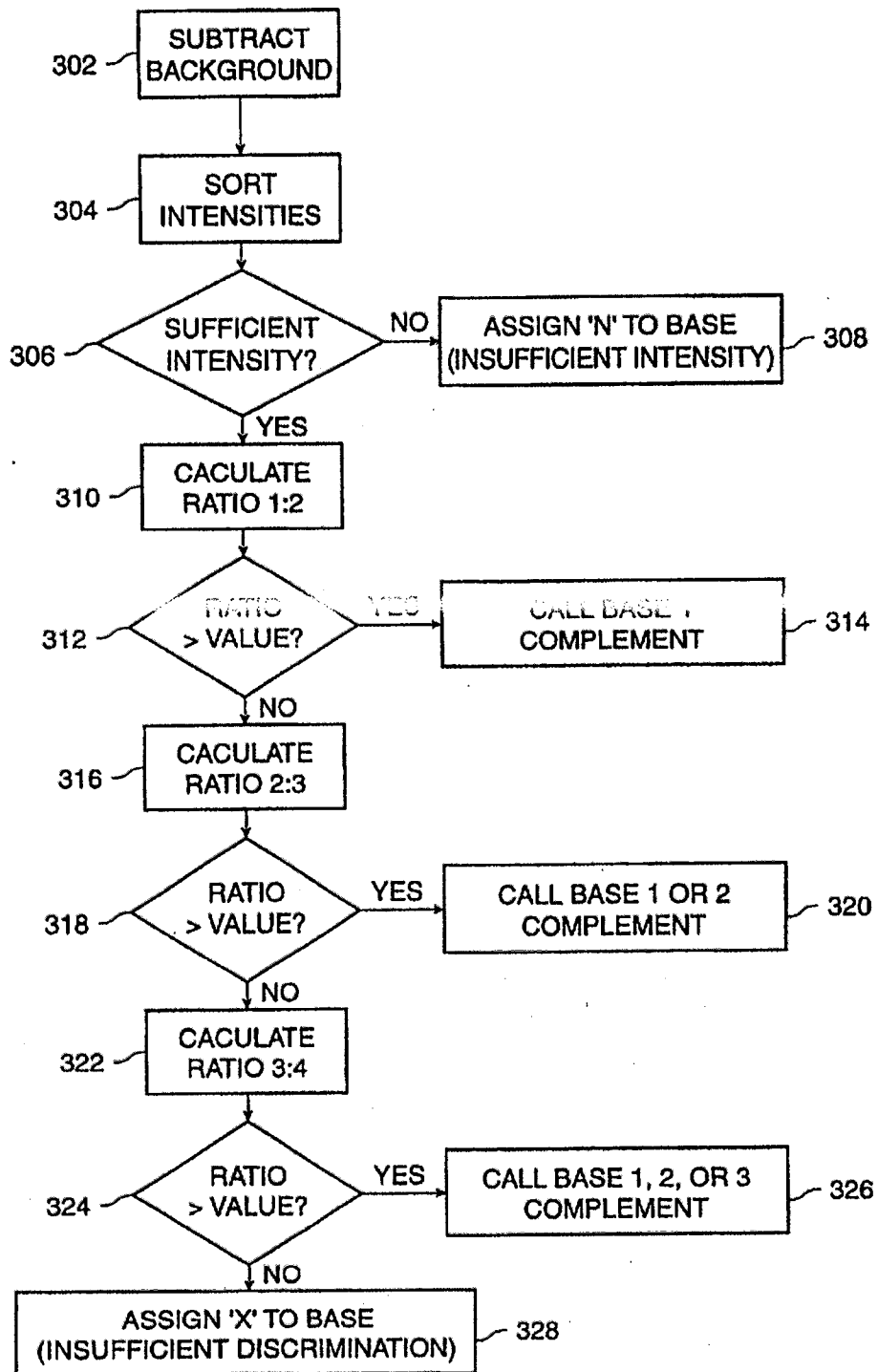


FIG. 3

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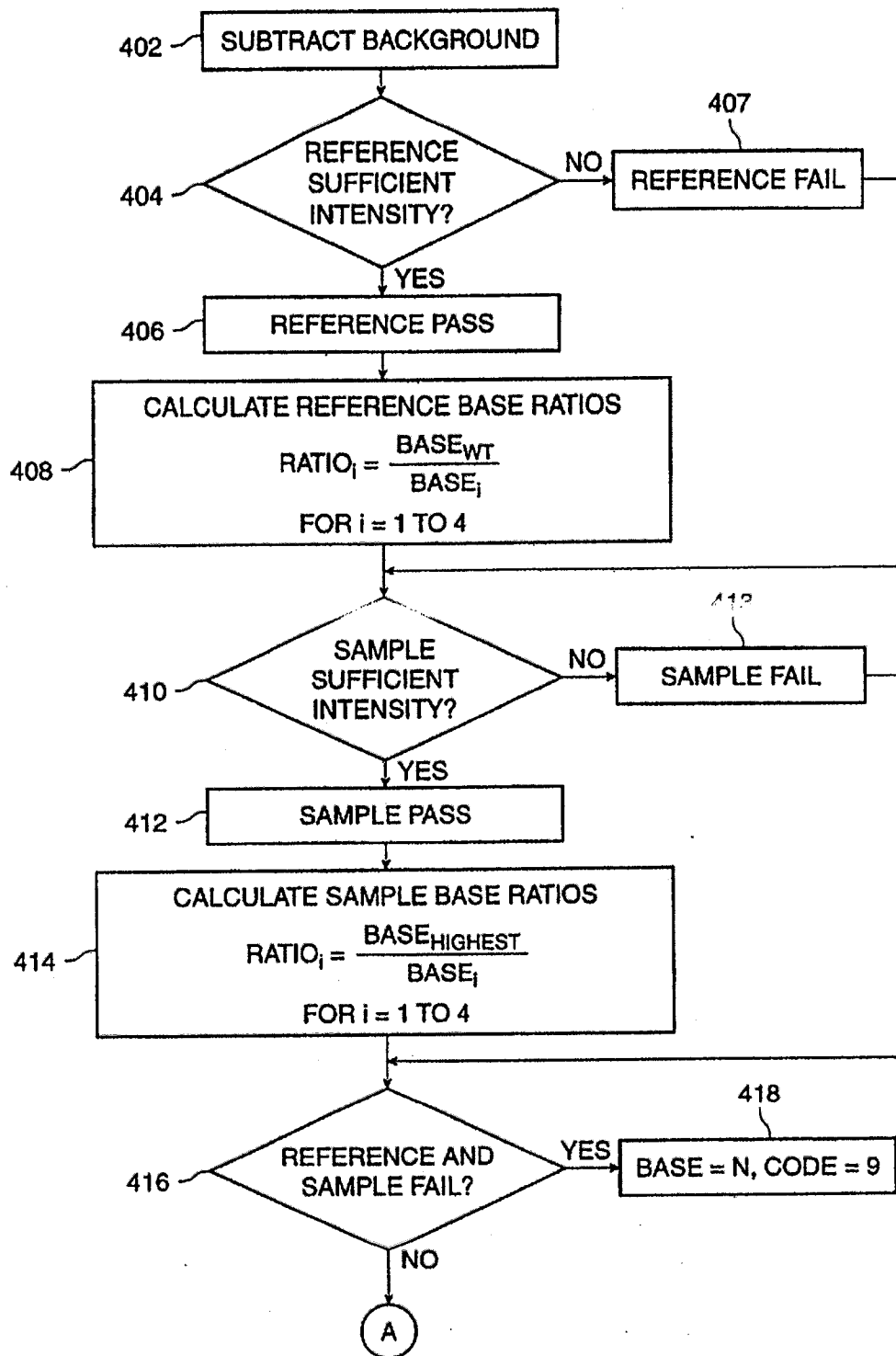


FIG. 4A-1

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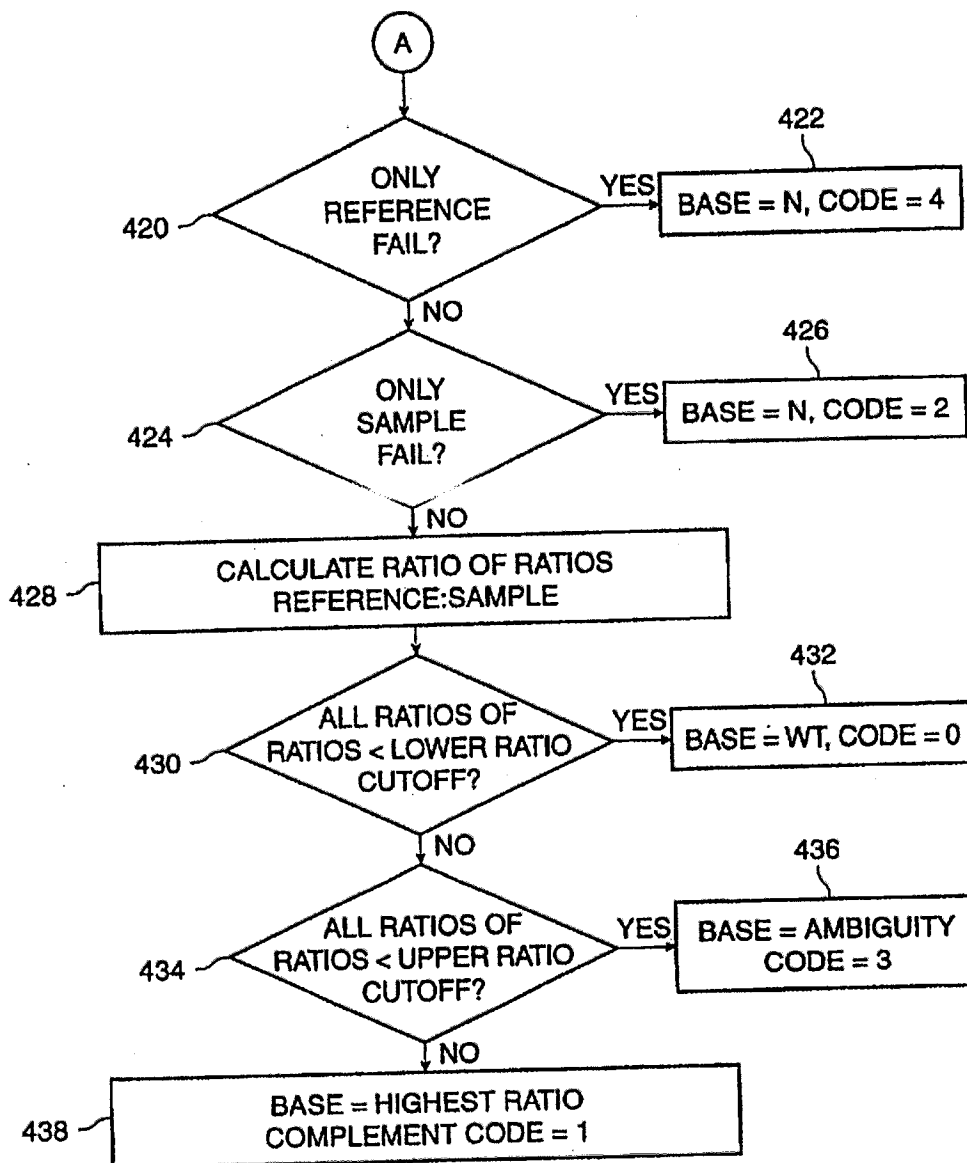


FIG. 4A-2



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		REFERENCE					SAMPLE					RATIO OF RATIOS							
POSITION	WT	BACK-GROUND		A	C	G	T	BACK-GROUND		A	C	G	T	A/A	C/C	G/G	T/T	BASE	CONFIDENCE
463	C	P	7.2	9.9	1.0	5.6	P	P	6.4	2.2	1.0	14.5	1.1	4.3	1.0	0.4	G	1	
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18		

FIG. 4B

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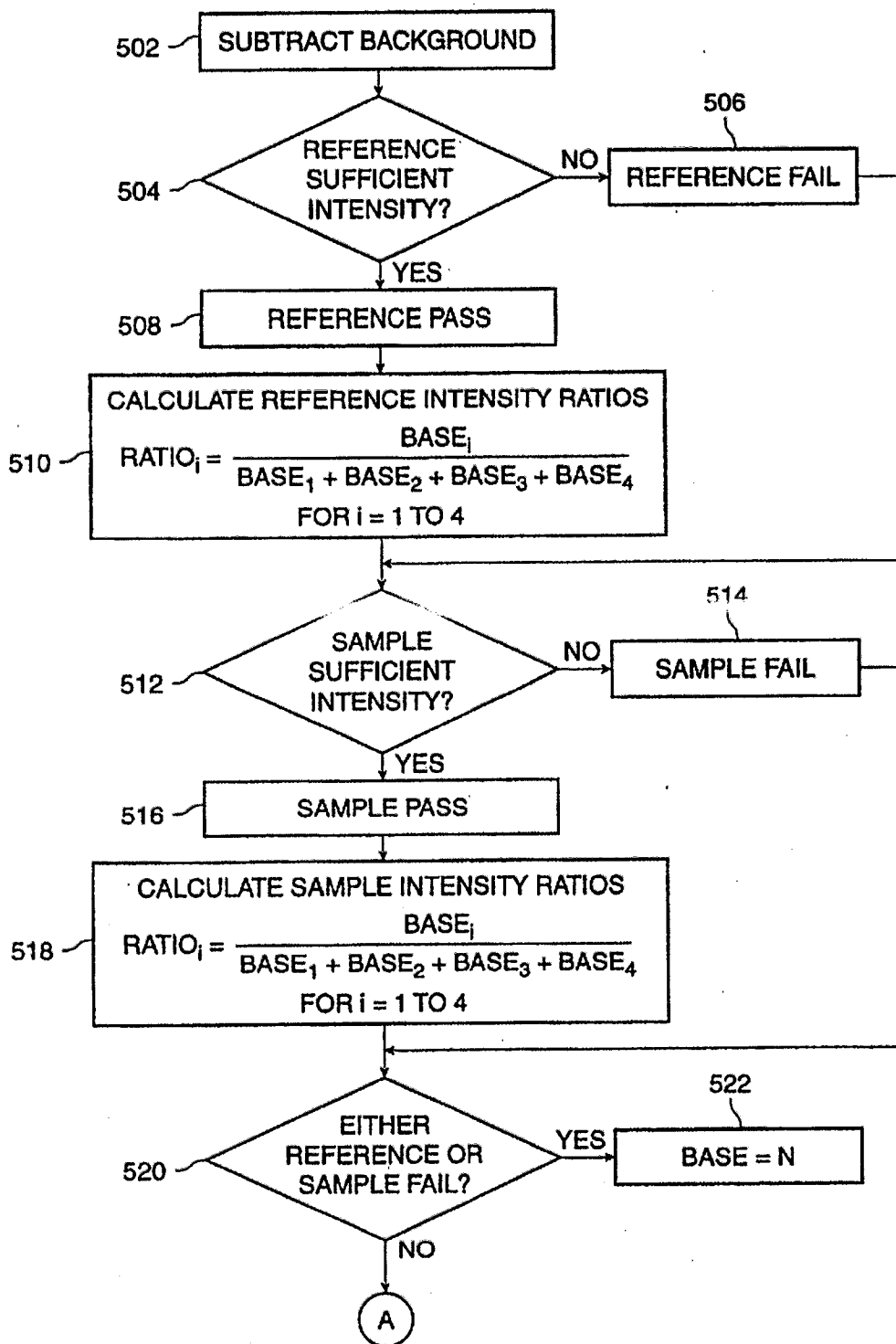


FIG. 5A-1

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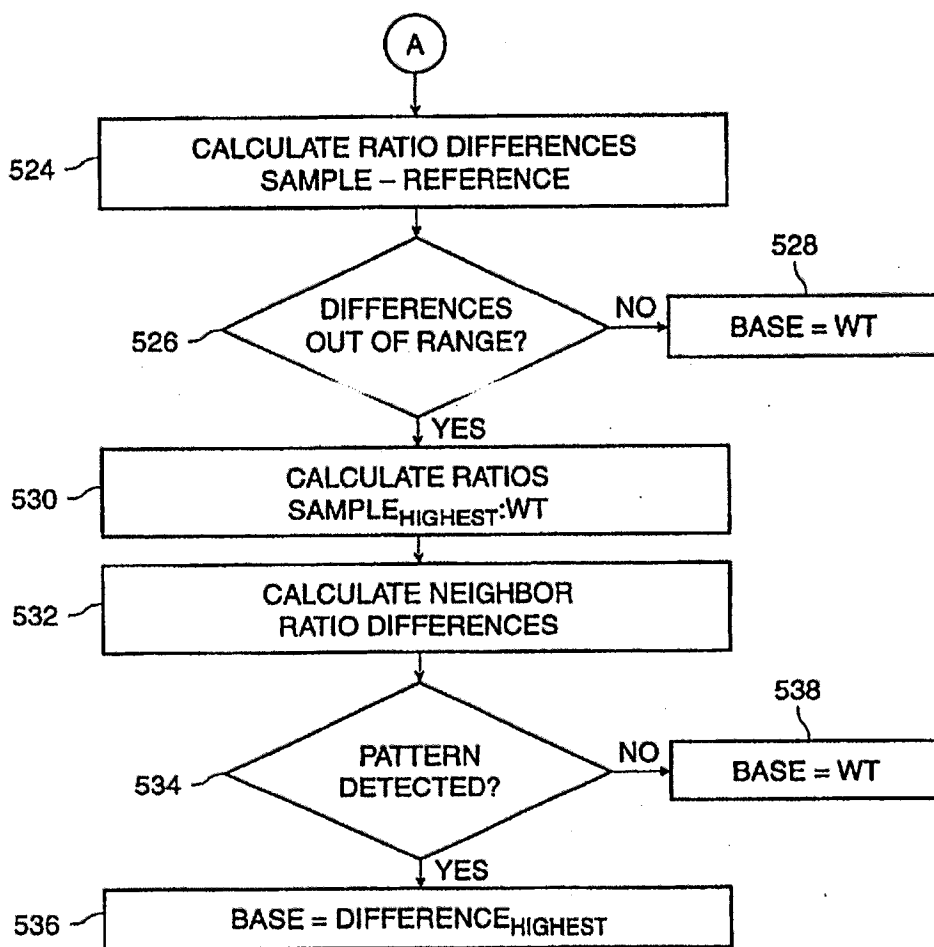


FIG. 5A-2

[illegible]

**FIG. 5B**

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BCK SUBTRACTED INTENSITIES																	502A										502B																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																									
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FIG. 5B-1

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WTEWTR	1.31	1.23	0.91	1.21	0.98	1.00	1.00	0.86	1.02	1.04	1.15	1.54	1.54	1.51	1.34	1.30	1.66
MAXEWTR	1.42	1.51	0.91	1.21	0.98	1.00	1.00	1.48	1.02	1.04	1.15	1.54	1.54	1.51	1.34	1.30	1.66
N-L + N-R		0.79	-0.63	0.54	-0.25	0.01	0.14	0.94	0.11	-0.10	-0.27	0.38	0.04	0.14	-0.13	-0.40	
N-L		0.09	-0.60	0.30	-0.24	0.02	0.01	0.48	-0.43	0.02	0.11	0.38	0.01	-0.04	-0.17	-0.04	
N-R		0.60	-0.30	0.24	-0.02	-0.01	-0.48	0.46	-0.02	0.11	-0.38	-0.01	0.04	0.17	0.04	-0.36	
N-L D(N-R)			-0.90	0.54	-0.25	0.01	-0.48	0.94	-0.43	-0.10	-0.27	0.38	0.04	0.14	-0.13		
N-R D(N-L)			-0.90	0.54	-0.25	0.01	-0.48	0.94	-0.43	-0.10	-0.27	0.38	0.04	0.14	-0.13		
L(N-L) - (N-R)L			0.29	0.07	0.22	0.02	0.49	0.02	0.44	0.13	0.50	0.39	0.03	0.21	0.21		
A+B-C			-2.10	1.01	-0.73	0.00	-1.44	1.86	-1.40	-0.33	-1.03	0.36	0.06	0.06	-0.48		
SUM MT/ SUM WT																	
INTENSITIES	2.16	1.88	1.15	1.39	1.41	1.39	1.31	1.95	1.52	1.20	1.30	1.60	1.71	1.78	1.50	1.45	1.63
N/L + N/R		2.50	1.45	2.18	2.04	2.05	1.61	2.77	2.04	1.71	1.89	2.18	2.03	2.22	1.88	1.85	
N-L + N-R		0.22	-0.48	0.10	0.02	0.03	-0.36	0.54	-0.03	0.21	-0.10	0.10	0.02	0.17	-0.11	-0.12	
N-L		-0.28	-0.73	0.21	0.03	-0.02	-0.09	0.54	-0.43	0.32	0.10	0.30	0.10	0.07	-0.27	-0.06	
N-R		0.73	-0.23	-0.03	0.02	0.09	-0.64	0.43	0.02	-0.10	-0.30	-0.10	-0.07	0.27	0.06	-0.18	

FIG. 5B-2

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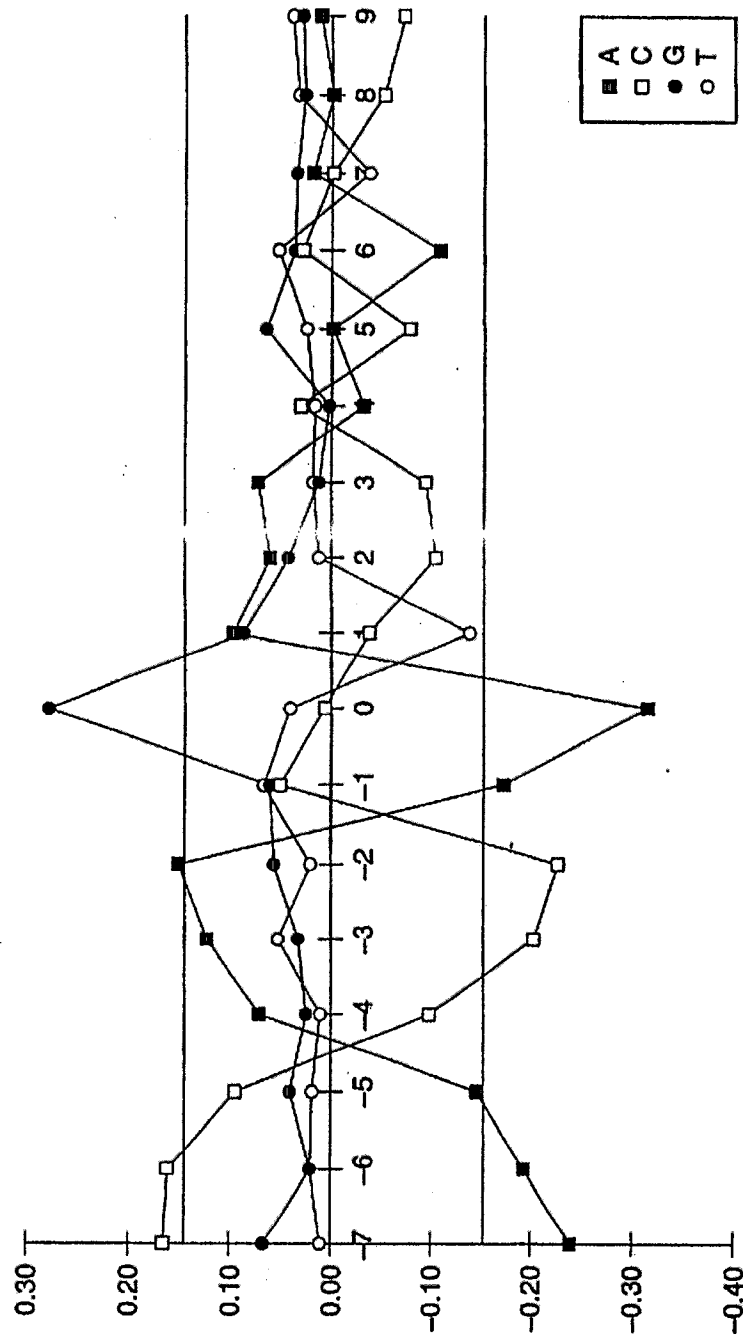


FIG. 5C

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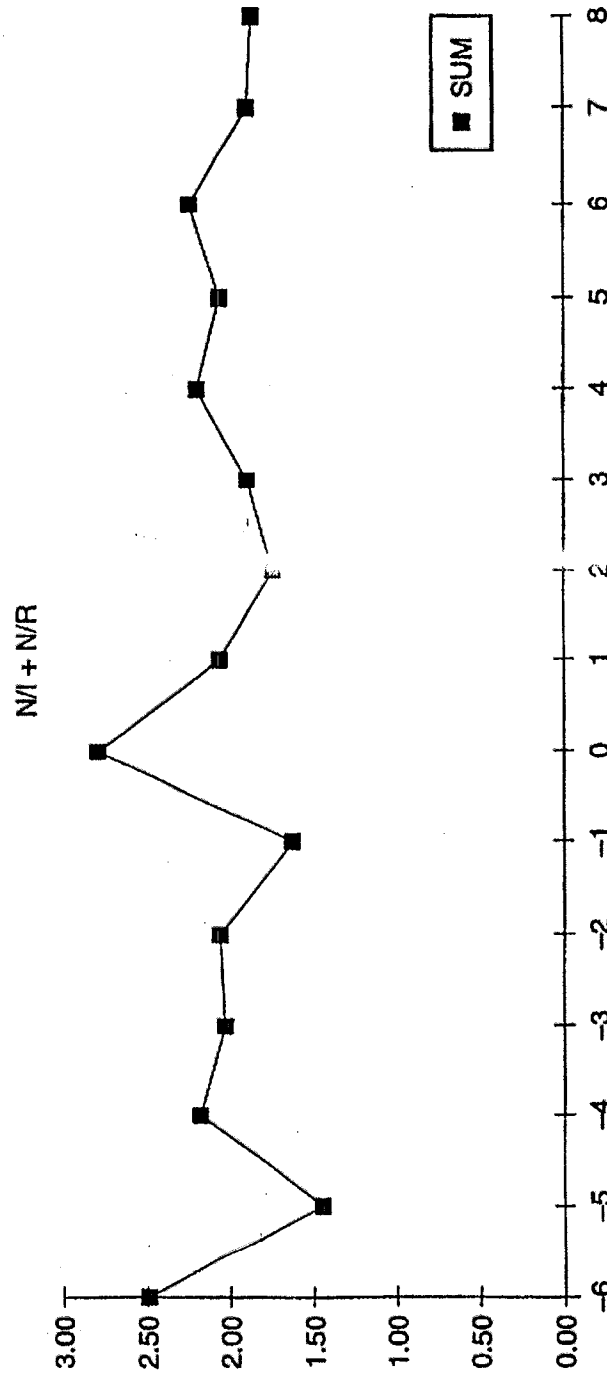


FIG. 5D



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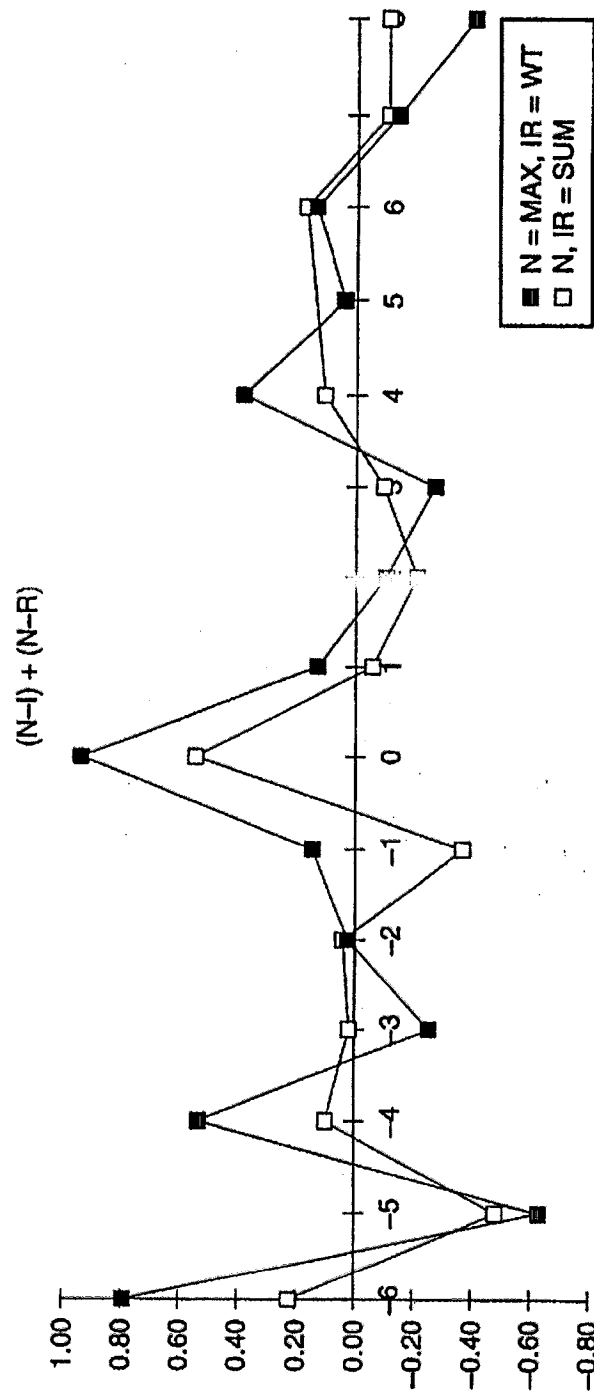


FIG. 5D-1